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EXAMINER

KERR, KATHLEEN M

ART UNIT PAPER NUMBER

1652

DATE MAILED: 11/04/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/858,332

Applicant(s)

TCHAGA ET AL.

Examiner

Kathleen M Kerr

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 April 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) 1-14 and 21-27 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 15-20 and 26-28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application):
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Application Status

1. In response to the previous Office action, a written restriction requirement (Paper No. 13, mailed on October 10, 2002), Applicants filed an election received on October 22, 2002 (Paper No. 14). Problems with the sequence listing precluded examination; however, these have been corrected to the point that examination is possible. Claims 1-28 are pending in the instant Office action.

Election

2. Applicant's election of Group IV, Claims 15-19 and 26-28, in Paper No. 14 is acknowledged. Said election was noted as being "with traverse"; however, because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (M.P.E.P. § 818.03(a)).

The Examiner notes that Claim 20 was inadvertently omitted from Group IV. Thus, Claims 1-28 are pending. Claims 1-14 and 21-25 are withdrawn from further consideration as non-elected inventions. Claims 15-20 and 26-28 will be examined herein.

Priority

3. The instant application is granted the benefit of priority for the U.S. Application Nos. 60/101,867 and 09/404,017 filed on September 25, 1998 and September 23, 1999, respectively, as requested in the first lines of the specification. The Examiner notes, however, that no disclosure of the claimed genus is found in either priority application. Thus, the pending claims

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are afforded an earliest effective filing date of May 15, 2001, the filing date of the instant application.

Information Disclosure Statement

4. The information disclosure statement filed on August 13, 2001 (Paper No. 4) has been reviewed, and its references have been considered as shown by the Examiner's initials next to each citation on the attached copy.

Oath/Declaration

5. Applicant has not given a post office address for inventor Jokhadze anywhere in the application papers as required by 37 C.F.R. § 1.33(a), which was in effect at the time of filing of the oath or declaration. A statement over applicant's signature providing a complete post office address is required.

Compliance with the Sequence Rules

6. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to **fully** comply with the requirements of 37 C.F.R. § 1.821 through 1.825; Applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990).

In the sequence listing filed on September 11, 2003 (by fax), wherein the CRF was filed prior, the paper copy and computer readable copy do not match as required. The paper copy

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contains 23 sequences while the computer copy contains only 20 sequences. Clarification and/or amendment are required.

If Applicants are amending the sequence listing, Applicants must provide some or all of the following: (1) a substitute copy of the sequence listing in both computer readable form (CRF) and paper copy, (2) an amendment directing its entry into the specification, (3) a statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. § 1.821 (e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d), and (4) any amendment to the specification to identify the sequences appropriately by SEQ ID NO.

Objections to the Specification

7. The specification is objected to for not teaching all the sequences from the sequence listing in the specification. SEQ ID NO:5 is described in the listing but can be found nowhere in the specification, as amended (an amendment on October 10, 2002 added the SEQ ID NO:5 descriptor while the amendment on February 4, 2003 deleted it). Clarification and/or correction are required.

8. The specification is objected to for a typographical error in the description of Figure 3 (as amended on February 4, 2003). SEQ ID NO:28 is indicated while no SEQ ID NO:28 is found in the sequence listing. The Examiner suggests considering SEQ ID NO:18 as the appropriate sequence. Correction is required.

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9. The specification is objected to because the title is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are drawn (see M.P.E.P. § 606.01). The Examiner suggests the following new title:

---Polynucleotides Encoding Metal Ion Affinity Peptides and Related Products---

10. In the specification, the Abstract is objected to for not completely describing the disclosed subject matter (see M.P.E.P. § 608.01(b)). It is noted that in many databases and in foreign countries, the Abstract is crucial in defining the disclosed subject matter, thus, its completeness is essential. The Examiner suggests the inclusion of the formulas in Claim 1. Since the art is replete with examples of metal ion affinity peptides, the only clear and accurate summary of the application must include the novelty, that is the sequence, for completeness.

Claim Objections

11. Claim 15 is objected to under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The polynucleotide in Claim 15 is a wholly distinct product, as noted in the previous restriction requirement, as is not a part of the subject matter of Claim 1.

12. Claims 15-20 and 26-28 are objected to for depending from non-elected claims. Incorporation of all the limitation of Claim 1 into Claim 15 is required.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 15-20 and 26-28 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The side chains in formulas 1 and 3 intended to be within the scope of the claims are unclear.

The term “aliphatic” side chain in the art typically refers to Ala, Val, Leu, or Iso since their side chains all have carbon and hydrogen and do not have other heteroatoms. Glycine has only hydrogen as its side chain; in the absence of a carbon atom, this side chain is not typically considered aliphatic in the art. However, on page 13, paragraph [0061], specific embodiments imply that Gly is intended to be included in this group. Thus, the metes and bounds of “aliphatic” are unclear.

The side chain “amide” is somewhat clear as Asn or Gln since these are in the embodiments and these are the only amide side chains in the 20 natural-occurring amino acids.

The terms “basic side chain (except His)” and “acid side chain” are unclear. In the art, Arg and Lys are clear as having basic side chains, and Asp and Glu are clear as having acidic side chains; these embodiments are implied on page 13, paragraph [0061]. The phrase “except His” is unclear since the pK_a of the proton on His is considered to be about 6, thus “acidic” or below pH 7 yet His is listed among the “basic” side chains. Clarification is required.

In all the above cases, it is unclear if these descriptors are referring to only naturally-occurring amino acids or not.

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Thus, the metes and bounds are unclear for all side chains in the claims when not specifically denoted by an amino acid name. The Examiner suggests careful, specific limitations of the optional amino acids at each position. The Examiner also suggests a different nomenclature in formula 3 since X_1 and X_2 in formula 3 are different from X_1 and X_2 in formula 1, yet these are in the same claim; the Examiner suggests X_7 and X_8 in describing formula 3.

The claims have been examined using the following parameters:

In Formula 1,

X_1 or X_2 = Ala, Val, Leu, Iso, Gln, Asn

X_3 or X_4 or X_5 = Arg, Lys, Asp, Glu

X_6 = Ala, Val, Leu, Iso, Gln, Asn

In Formula 3,

X_1 or X_2 = Asp, Glu

Correction and/or clarification are required.

14. Claim 16 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "amino- or carboxy-terminus" is unclear as to whether the affinity sequence must be at the end of the sequence (NH_3 -formula 1) or merely near the end of the sequence (NH_3 -X-X-X-formula 1). If the affinity sequence need only be near the end of the polypeptide, how close must the affinity sequence be to the end? Clarification is required.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

15. Claims 15-19 and 26-28 are rejected under 35 U.S.C. § 102(b) as being anticipated by Chaga *et al.* (Natural poly-histidine affinity tag for purification of recombinant proteins on cobalt(II)-carboxymethylaspartate crosslinked agarose. J. Chromat. (1999) 864:247-256). The instant claims are drawn to a polynucleotide that encodes a fusion polypeptide having formula 1 near its N-terminus, vectors and *E. coli* host cells thereof, and affinity purification kits thereof.

Chaga *et al.* teach a poly-histidine affinity tag (HAT) fused to CAT (chloramphenicol acetyltransferase), DHFR (dihydrofolate reductase), and GFPuv (green fluorescent protein – UV-enhanced variant) in a vector wherein the HAT sequence is Lys-Asp-(His-Leu-Ile)-(His-Asn-Val)_{n1}-(His-Lys-Glu-Glu)_{n2}-(His-Ala)-(His-Ala)-(His-Asn)_{n3}-Lys (the underlined portion meets the requirements for formula 1) (see Figure 1). Chaga *et al.* teach expression of the HAT-tagged proteins in *E. coli* host cells, DH5α (see Abstract). Chaga *et al.* also teach metal ion affinity resin, carboxymethylaspartate superflow, in a column and extraction, wash, and elution buffers (see Figure 2).

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16. Claims 15 and 17-20 are rejected under 35 U.S.C. § 102(e) as being anticipated by Sato (USPAP 2003/0079237A1 filed June 7, 1999). The instant claims are drawn to a polynucleotide *comprising* a nucleotide sequence that encodes (His-Asn)₃ (formula 2 with n=3) and vectors and prokaryotic and eukaryotic host cells.

Sato teaches a nucleic acid molecule that encodes mouse p75NTR (NADE); the sequence of mouse NADE comprises an internal fragment: His-Asn-His-Asn-His-Asn (see Figure 1A) that meets the limitations of formula 2. Sato also teaches vectors (see paragraph [0137]) and prokaryotic and eukaryotic host cells (see paragraph [0143]) of the mouse NADE DNA sequence.

17. Claims 15 and 17-19 are rejected under 35 U.S.C. § 102(b) as being anticipated by Giraldo *et al.* (Characterization of a *Plasmodium chabaudi* gene encoding a protein with glutamate-rich tandem repeats. Parasitology Research (1999) 85:41-46) as evidenced by GenBank Accession Number AF019972 (*Plasmodium chabaudi* NE-rich protein gene, March 23, 1999). The instant claims are drawn to a polynucleotide *comprising* a nucleotide sequence that encodes (His-Asp-Glu)-(His-Asp-Glu)-(His-Asp-Glu) (formula 3 with X₁-X₂ as noted above, n=3).

Giraldo *et al.* teach a polynucleotide encoding an NE-rich protein and its expression, using a vector, in *E. coli*, a prokaryote (abstract and see page 42). The sequence of the NE-rich protein has an internal sequence of His-Asp-Glu-His-Asp-Glu-His-Asp-Glu from residues 311-320 as evidenced by GenBank Accession Number AF019972.

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Other References Cited

18. The following references are cited to complete the record:

- a) Chaga *et al.* Immobilized metal ion affinity chromatography of Co^{2+} -carboxymethylaspartate-agarose Superflow, as demonstrated by one-step purification of lactate dehydrogenase from chicken breast muscle. *Biotechnol. Appl. Biochem.* (1999) 29:19-24.
- b) Zhang *et al.* USPN 5,670,483 teaches a $(\text{His-Asn})_x$ peptide as an affinity peptide (see Table 2, item HN16, SEQ I DNO:53) but do not teach DNA encoding the peptide; the peptides throughout Zhang *et al.* are made by peptide synthesizers, not for fusion proteins.

Conclusion

19. Claims 15-20 and 26-28 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 9:00am to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

KMK

November 3, 2003

